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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,732	11/20/2000	Richik N. Ghosh	97,022-N2	8004
20306	7590	11/18/2004	EXAMINER	
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP			COOK, LISA V	
300 S. WACKER DRIVE			ART UNIT	
32ND FLOOR			PAPER NUMBER	
CHICAGO, IL 60606			1641	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/716,732

Applicant(s)

GHOSH ET AL.

Examiner

Lisa V. Cook

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21, 22 and 26-32 is/are rejected.
- 7) ☒ Claim(s) 23-25 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Request for Continued Examination***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 June 2004 has been entered.

***Amendment Entry***

2. Applicant's amendment and response to the Final Office Action mailed 25 March 2004 is acknowledged. In the Amendment filed therein claims 21, 25-27, and 29 were modified. Currently claims 21-32 are pending and under consideration.

**REJECTIONS MAINTAINED**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 21-32 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 21 is vague and indefinite because it is not clear as to how the nuclear image and the neurite image will be employed to measure neurite outgrowth. The claims merely requires two separate imaging of the nucleus and neurite but does not identify how the images will be related to each other or will measure neurite outgrowth. Please identify the relationship between the two images.

B. Claim 21 step d) recites the limitation "the cell bodies from the neurite image" in step b). However claim 21 step b) does not include "cell bodies". There is insufficient antecedent basis for this limitation in the claim. Step d) should read "a cell body" in order to obviate the rejection.

C. In claim 22 the use of "cell bodies" is not clear because it is not clear if applicant intends to mean the cell bodies in claim 21 step c) or claim 21 step d). Appropriate correction is required.

D. In claim 28 the use of "cell bodies" is not clear because it is not clear if applicant intends to mean the cell bodies in claim 21 step c) or claim 21 step d). Appropriate correction is required.

***Response to Arguments***

Applicant contends that the claims clearly set forth that the neuritis identified in 21(d) extend from the cell bodies which were identified in the nuclear image in 21(c). Arguments presented in response filed June 23, 2004 - on page 4, 4<sup>th</sup> paragraph – on page 5, 2<sup>nd</sup> and 4<sup>th</sup> paragraphs – on page 6 6<sup>th</sup> paragraph. However, this limitation is not clearly recited in the claims. The rejections above are maintained. The claims merely read on two different measurements one in 21(c): nuclear image and another in 21 (d): neurite image. It is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

**NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT**

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 21, 26-27, 29, and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (Cytometry 25:71-81, 1996) in view of Lieske et al. (Neuroscience, Vol.90, No.3, pages 967-974, 3/9/99) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only).

Dow et al. teach automatic multiparameter fluorescence imaging. Thin tissue sections were stained with Hoechst and three different fluorescent antibodies to antigens that allowed for typing and evaluation of T-cells. This procedure provided the spatial relationships (location) of multiple cell types simultaneously within the tissue. See abstract. The procedure provided an array of locations comprising cells. See figure see for example.

In order to measure the expression of multiple antigens in the sample a first image of the DNA (nuclear material) was employed to identify each nucleated cell and its nuclear boundary. Applicant's nuclear image. In the second step the antibody bound antigen image was used to measure deformable splines in each antigen image. See page 72 1<sup>st</sup> column. The deformable splines initially positioned at the Hoechst-stained nuclei or nuclear boundaries (cell bodies) are applied to images of the fluorescently labeled cell surface antigen cell boundary (cell bodies). From the measurements acquired at this boundary (cell bodies) each cell is classified according to antigen expression. See abstract, page 75, and page 76.

This analyses was employed to study cell infiltrate in melanoma tissue sections pre and post treatment (at multiple time points). In this way activated and quiescent cytotoxic and helper T-cells were identified simultaneously in single sections. Page 79 - 2<sup>nd</sup> column last paragraph. Dow et al. also disclose multiple imaging (images taken in a series) as a means of optimizing the focus. Page 73 Column 1, 3<sup>rd</sup> paragraph.

Although Dow et al. are silent with respect to the label being a luminescent label it is noted that the type of label employed is deemed mere optimization of the method taught by Dow et al. Absent evidence to the contrary the use of a luminescent label is an obvious design choice routinely modified in the art. This view is supported by the abstract of Wang et al. wherein luminescence labels and fluorescence labels are taught to be interchangeable.

Dow et al. differs from the instant invention in not specifically teaching the detection of neurite outgrowth.

However, Lieske et al. disclose that neurite outgrowth can be assessed by image analysis. See abstract and page 968. Specifically more than 500 neurons from cultured experiments were evaluated with respect to neurite length “21 v)” and the total number of neuritis per cell “21 iii)”. See page 968 1<sup>st</sup> column 4<sup>th</sup> paragraph. This assessment is useful in determining cortex development and potential effectors of cortex development (5-HT). See page 967 1<sup>st</sup> column 1<sup>st</sup> paragraph. The quantitative analysis of 5-HT exhibits significant changes on cell body outgrowth, neuritis, and dendrites. Please see page 969 2<sup>nd</sup> column 3<sup>rd</sup> paragraph through page 971 1<sup>st</sup> column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure neurite outgrowth as taught by Lieske et al. in the method of Dow et al. because Lieske et al. taught that neurite outgrowth imaging was useful in evaluating effectors of cortex development. See abstract and page 967 1<sup>st</sup> paragraph.

Therefore one of ordinary skill would be motivated to measure neurite outgrowth images as taught by Lieske et al. in the method of Dow et al. in order to evaluate neurological disorders (cortex development).

One of ordinary skill would have expected the combination of Dow et al. in view of Lieske et al. to be successful because both references teach cell imaging analysis procedures.

II. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (Cytometry 25:71-81, 1996) in view of Lieske et al. (Neuroscience, Vol.90, No.3, pages 967-974, 3/9/99) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) and in further view of Ranefall et al. (Analytical Cellular Pathology, 15, 1997, 145-156).

Please see Dow et al. (Cytometry 25:71-81, 1996) in view of Lieske et al. (Neuroscience, Vol.90, No.3, pages 967-974, 3/9/99) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) as set forth above.

Dow et al. (Cytometry 25:71-81, 1996) in view of Lieske et al. (Neuroscience, Vol.90, No.3, pages 967-974, 3/9/99) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) differ from the instant invention in not specifically teaching nuclear imaging including dilations of the kernel (central or initial nuclear image for further identification).



Ranefall et al. disclose that segmented images (dilations of the kernel image) of stained nuclei can distinguish positive staining reaction from other cell nuclei. See abstract. The full nuclear image is split and spread to more clearly identify the stained cells. See page 146.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure segmented images (dilations of the kernel image) of stained nuclei as taught by Ranefall et al. in the method of Dow et al. in view of Lieske et al. as supported by Wang et al. because Ranefall et al. taught that this procedure improved reproducibility and more accurately identified positive nuclei. Page 155 Discussion.

III. Claims 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (Cytometry 25:71-81, 1996) in view of Lieske et al. (Neuroscience, Vol.90, No.3, pages 967-974, 3/9/99) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) and in further view of Sano (Current Trends in Neurochemistry, 1997, Vol.1, pages 27-40 Abstract Only).

Please see Dow et al. in view of Lieske et al. as supported by Wang et al. as set forth above.

Dow et al. in view of Lieske et al. as supported by Wang et al. differ from the instant invention in not specifically teaching the contacting of the cells with a control compound to stimulate neurite outgrowth and further analyze a tests compounds ability to inhibit neurite outgrowth.

However, Sano disclose this limitation. Specifically, Sano teach the utility of PC12 cells, which are NFG-dependent for neurite outgrowth. A MEK inhibitor - PD-98059, inhibited the neurite outgrowth. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure neurite outgrowth with a control compound to stimulate said outgrowth and further analyze a test compound for inhibition as taught by Sano in the method of Dow et al. in view of Lieske et al. as supported by Wang et al. because Sano taught that this procedure provided predictable neurite outgrowth that allowed for discrimination of inhibitor pathways. See abstract.

#### ***Response to Arguments***

Examiner acknowledges that Wang et al. is not prior art against the instant application. The reference to Wang et al. was merely cited as support for the art recognized interchangeability of luminescence labels and fluorescence labels.

The test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See, *In re Bent*, 52 CCPA 850, 144 USPQ 28(1964); *In re Nievelt*, 179 USPQ 224 (CCPA 1973).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Arguments directed to the reference of McFarlane et al. are MOOT, because the reference has been replaced with Lieske et al. (Neuroscience, Vol.90, No.3, pages 967-974, 3/9/99). McFarlane et al. taught neurite length from all cells. This limitation has been removed from the claims.

Accordingly, Lieske et al. has been added for teaching cell body measurements as well as the number of neuritis and neurite length per cell. Please see page 969 2<sup>nd</sup> column 3<sup>rd</sup> paragraph through page 971 1<sup>st</sup> column.

With respect to Dow teaching “splines” as image processing techniques on page 76 left column, lines 6-11, it is noted that the passage does not recite “splines”. Nuclear area (cell bodies) imaging via two-dimensional segmentation is taught.

All the rejections have been reconfigured to include Lieske et al. Therefore the deficiencies noted in the combination of Dow et al. in view of McFarlane et al. for reasons of record in paper #14 have been addressed.

***Allowable Subject Matter***

5. Claims 23-25 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

6. For reasons aforementioned, no claims are allowed.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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REMSEN 3C-59

Art Unit 1641

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8/3/04



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